

Neuropathology of Hashimoto's encephalopathy

Doherty *et al* have recently reported in this journal on a case of Hashimoto's encephalopathy clinically mimicking Creutzfeldt-Jakob disease.¹ As neuropathological analysis of a brain biopsy in this case revealed spongiform change and sparse mononuclear infiltrates in perivascular spaces, the authors suggested that Hashimoto's encephalopathy is an encephalitic process. We have previously described a necropsy case of Hashimoto's encephalopathy showing lymphocytic vasculitis of veins and venules of the brain stem, supporting the hypothesis that vasculitis represents the morphological substrate of Hashimoto's encephalopathy.² Doherty *et al* have challenged our diagnosis and stated that the term vasculitis should be reserved for lesions with inflammation and fibrinoid necrosis of arterial vessels.

Lymphocytic vasculitis is a generally accepted pathological subtype covered by reviews and standard textbooks.^{3,4} It is characterised by the presence of lymphocytes within the vessel wall and is encountered in Wegener's disease, systemic lupus erythematosus, and Behcet's disease, to name but a few conditions.⁴ That the diagnosis is more difficult than for necrotising arteritis does not, however, imply that lymphocytic vasculitis does not exist, and our case certainly belongs in this vasculitis category.

Additional support for the vasculitic basis of Hashimoto's encephalopathy comes from other reports on this condition where there has been angiographic demonstration of vasculitis.⁵ More recent experimental evidence for a vasculitic pathogenesis involves the identification of α -enolase as an autoantigen in Hashimoto's encephalopathy,⁶ because anti- α -enolase antibodies are present in various autoimmune vasculitic diseases such as systemic lupus erythematosus and ANCA associated vasculitis, and because α -enolase is highly expressed in the endothelium.

Based on the histological figure and the description provided by Doherty *et al*,¹ we express some reservations over the presence of "spongiform" changes. True spongiform changes, usually encountered in prion diseases, are present in the neuropil between nerve cell bodies, whereas the perineuronal spaces illustrated by Doherty *et al* more closely resemble shrinkage artefacts which may be particularly pronounced in small biopsy specimens. In addition, we would like to point out that vasculitis is typically focal and may have been missed in this case.

In conclusion, we feel that the available clinical, pathological, and experimental evidence suggests that vasculitis underlies a substantial proportion of cases of Hashimoto's encephalopathy. However, additional careful necropsy studies are required to determine whether other pathologies contribute to the clinical picture.

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Authors' reply

We thank Drs Paulus and Nolte for their interest in our case report, which we offered as a lesson in the clinical, and to a certain extent pathological, similarities between Creutzfeldt-Jakob disease (CJD) and Hashimoto's encephalopathy on small biopsies. Of course, in established CJD—as the correspondents rightly mention—spongiform change is easily recognised by vacuoles in the neuropil; in contrast to their contention, these are regularly accompanied by neuronal cytoplasmic vacuoles displacing surrounding neuropil (similar to those we illustrated), as described in standard textbooks¹ and in clinicopathological cases.² The difficult judgment is in the brain biopsy in early CJD, in which these changes are minimal and indeed nearly impossible to distinguish from artefact or oedema. The concurrence of astrogliosis with the spongiform appearance (no matter what the cause) in our case further lowered our threshold for submitting the tissue for definitive prion protein studies in the clinical setting of rapidly evolving cognitive decline. We hope the correspondents would agree that such would be simply good clinical practice, especially in a patient like ours without a helpful history of Hashimoto's thyroiditis or anti-thyroid peroxidase antibodies.

As to their assertion that we "challenged" their diagnosis of vasculitis (which we point out was followed by a question mark in the title of their own report!), we felt that the previous subarachnoid haemorrhage and apparently diffuse lymphocytic infiltration of the leptomeninges that they described suggested that the venular lymphocytic infiltrates could be secondary to the haemorrhage, or be a manifestation of a meningoencephalitis (possibly autoimmune) rather than a true primary vasculitis.³ According to the textbook they cite, the entities of Wegener's disease, systemic lupus erythematosus, and Behcet's disease, to use their examples, are all characterised primarily by true arteritis with necrosis, not by the lymphocytic venulitis which may accompany it.⁴ Drs Paulus and Nolte are correct that in our small biopsy, vasculitis may have been missed. They may also be correct that the pathogenesis of Hashimoto's encephalopathy involves vasculitis. We stand firm in our position, however, that to make a histological diagnosis of vasculitis requires the exclusion of other factors, such as haemorrhage or tissue inflammation, in which lymphocytic diapedesis through venules is physiological. Moreover, the novel finding in our case of parenchymal inflammation does raise the prospect of an encephalitic process in Hashimoto's encephalopathy, independent of any effect on blood vessels, whether primary or secondary.

We thank Drs Paulus and Nolte for pointing out the interesting paper by Ochi *et al*,⁵ and look forward to future elucidation of the role of α -enolase in Hashimoto's encephalopathy. Perhaps those of us with tissue from cases of Hashimoto's encephalopathy will need to col-

laborate in that regard, to expand their studies on serum from patients with this condition.

Finally, we want to reiterate the importance of a broad differential diagnosis in evaluating patients with rapid decline in cognition, and with vacuoles, astrogliosis, microgliosis, and parenchymal perivascular mononuclear cells on brain biopsy. That was the overarching point of our paper.

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BOOK REVIEWS

Management of stroke: a practical guide for the prevention, evaluation and treatment of acute stroke, 2nd edition

Edited by Harold P Adams, Gregory J del Zoppo, and Rudiger von Kummer (Pp 303, US\$24.95). Published by Professional Communications Inc, Caddo, 2002. ISBN 1-884735-517

This textbook exemplifies the recent and dramatic changes in the approach to the management of acute stroke. Whereas in the past stroke was seen as untreatable, this book sees stroke as an emergency warranting acute treatment. As the authors state in the introduction, "A positive attitude towards stroke is critical. Patients with cerebrovascular disease should be considered to have an illness that can be treated successfully." This admirably emphasises the approach that sees stroke not as an untreatable "cerebrovascular accident" (a term that should be expunged from medical texts) but as a "brain attack", a term the authors use to emphasise the need for rapid diagnosis and evaluation of acute suspected stroke.

Despite giving the impression of being a brief guide, almost all aspects of emergency stroke treatment are covered, starting with organisation of stroke services and proceeding to diagnosis and emergency treatment. There is also a chapter devoted to stroke prevention. The text is divided into 13 chapters, followed by a reference list and an index, which includes the tables and figures. The text is illustrated with computed tomography and magnetic resonance imaging scans and is interspersed throughout with very helpful

summary tables. Advice is clearly given and where there is controversy, the authors do not hesitate to discuss both sides of the argument. There is an emphasis on medical care during the first few days after a stroke. Rehabilitation is quite rightly introduced as an integral part of the management of patients with stroke, but not really explored, being only allocated a few paragraphs. Hence, the book is clearly not intended to be a comprehensive guide to the totality of multidisciplinary acute stroke management.

Measuring only 6 × 4 × 2 cm, this book is small enough to fit in a white coat pocket. This suggests that the book is designed to be carried around by the medical student, resident, or trainee on acute take. However, nowhere in the book do the authors make clear their intended audience and neither do they say whether it is intended to be a pocket sized handbook or a detailed textbook that happens to be small. Certainly the size of the book is an advantage, and the numerous tables will undoubtedly prove useful for the busy clinician or the student revising for exams. However, the lack of colour detracts from the attractiveness of the text and the binding prevents the book from opening well. It also needs a more durable cover as it will quickly become dog-eared from being frequently stuffed in and out of a pocket.

Unusually for this type of book, the text is extensively referenced, with 688 separate references, reflecting the large evidence base behind the current rational treatment of stroke. This has the disadvantage that references after nearly every sentence tend to interrupt the flow of text, giving the impression that one is reading a list of facts. If the text is really meant to be used to guide treatment in the heat of the moment, or equally to be read at leisure to gain understanding of the topic, perhaps a recommended reading list of a few key articles at the end of each chapter might be more useful.

The text is clearly orientated towards the North American market. For example, it is assumed that suitable patients will be treated with intravenous tissue plasminogen activator (tPA). This has not yet been licensed in most other parts of the world, but the algorithm detailing the assessment of patients with thrombolysis will prove useful elsewhere when tPA eventually receives a license outside North America. The text does deal with many other acute approaches to treatment that can be adopted without embracing thrombolysis, for example the treatment of metabolic disturbances and raised intracranial pressure. Another difficulty is that the use of some North American terms may grate slightly with those more used to other forms of English. For example, 'emergent' rather than 'emergency' is used throughout. Some North American terms such as emergency department are written in full only once, then used abbreviated (ED) throughout the book. A list of the many abbreviations would help with this problem.

In conclusion, this is a useful book on acute stroke management, which will appeal especially to the North American market. The next edition will hopefully be more user-friendly with a better layout, improved binding, and some colour.

Z E Brown, M M Brown

Diseases of the nervous system: clinical neuroscience and therapeutic principles

Edited by A K Asbury, G M McKhann, W I McDonald, *et al.* Cambridge University Press, Cambridge 2002, £250.00, 11 volumes. ISBN 0-521-79351-3

The third edition of this well known book is subtitled *Clinical neuroscience and therapeutic principles*. This signifies that it is not a textbook of clinical practice, but a reference book founded in pathophysiology. So how well does it succeed? With 221 authors writing 129 chapters some unevenness is inevitable. It is a tribute to the editors' tight grip that the overall coverage of neurological disease is suitably comprehensive.

I particularly liked the introductory section which highlights contemporary trends in understanding neurological disease processes, the principles of restoring function after damage, and "windows on a working brain". This is the section of the book that I chose to read for pleasure, simply for a succinct and thoughtful view as to where neurology is going outside my own subspecialty. And throughout the book, there is excellent coverage of background issues ranging from the chemical bases of addiction and alcoholism, to host responses to infection, to pathophysiology of cerebral circulation, to the cellular basis of epilepsy, and to repeat trinucleotide expansions.

Inevitably one can take issue with aspects of subject matter coverage, particularly in one's own subspecialty. For instance, within the neuromuscular disease section, the scientifically interesting and clinically important multifocal motor, CIDP, paraproteinaemic, and vasculitic neuropathies, lie buried incognito in a chapter entitled "Guillain-Barré syndrome". I imagine that the lack of coverage of mononeuropathies deliberately reflects the lack of sexy science underlying this topic, despite its commonness as a clinical encounter. Most welcome, is the coverage of how channelopathies and metabolic derangements affect muscle function.

Although extending to two hefty volumes, totalling over 2000 pages, this text has a refreshingly light and accessible feel. The index is reasonably good. Many of the illustrations are line drawings, and are beautifully clear. This enhances the notion of scientific principles which imbues the text. A superb book to have at hand in one's office alongside a textbook of clinical practice. It is pretty expensive, but probably worth it if you need a succinct summary of the myriad bases for neurological disease.

M Donaghy

Fighting for mental health. A personal view

N Sartorius. Cambridge University Press, Cambridge, 2002, £29.95, pp 266. ISBN 0 521 58243 1

This volume is a collection of essays and articles written by Norman Sartorius, the very eminent and influential psychiatrist. Fighting for Mental Health in Professor Sartorius' judgement means fighting on three fronts—

ensuring that psychiatric practice is based on evidence and experience, that it is part of medicine and develops mutually supportive relationships with it, and that it grows in conjunction with overall socio-economic development. The book is divided into three parts addressing each of these three themes. There is a wealth of stimulating, challenging, and elegant argument used in so doing, and whether one agrees or disagrees with any particular premise the clarity of thought is enviable. Inevitably in a collection such as this there is some degree of repetition and, to some extent, a difficulty in maintaining a focus on the overarching themes and concepts. Nevertheless the book amply repays the time spent in reading each essay carefully and thoughtfully, and it is a great pleasure to recognise Professor Sartorius' passion for the wellbeing of people with mental health problems. Each chapter of the book is illustrated by a very carefully selected painting and each of these adds another dimension to the work.

At the end of his introduction Professor Sartorius urges psychiatrists to "fight the social and political battles that are necessary to improve the fate of people struck by mental illness, and make psychiatry and related disciplines and sciences useful to society and responsive to its ethical duties". This is a rallying call which I hope will be heard and responded to by many.

J Hollyman

Essential pharmacology of antipsychotics and mood stabilizers

By Stephen M Stahl (Pp 152, £24.95). Published by Cambridge University Press, Cambridge, 2002. ISBN 0-521-89074-8

This short book is an update of the two chapters from the second edition of Stahl's larger textbook *Essential pharmacology* that deal exclusively with psychosis and schizophrenia and their treatment with antipsychotic drugs. The author argues that this new book is justified by the rapidly expanding knowledge base of psychopharmacology for psychosis and schizophrenia.

This book has the same qualities as its big brother. The simple and beautifully conceived graphics make the book highly readable while conveying information that is at the cutting edge of contemporary neuroscience. The latest theories of mechanisms of "atypicality" are presented, including Kapur's rapid dissociation theory, as are the modes of action of the new generation of so-called dopamine system stabilisers, exemplified by aripiprazole. Given that the latter has not yet been launched in the UK, this volume can truly claim to be ahead of the field. There is less new information on mood stabilisers, although some extended discussion of the use of atypical antipsychotics in mood disorders.

Those who already have a copy of *Essential pharmacology* may be tempted to upgrade. New readers may be drawn to a thin, attractively presented volume. However, some concern must be expressed at the practice of releasing new material in this way. This book is not cheap for its size and the third edition of *Essential pharmacology* cannot be far behind.

C Bench